Use of Radioactive Chromic Phosphate in Pleural Effusions

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• Radioactive chromic phosphate was chosen in place of radioactive gold for control of pleural effusions and ascites.

The chromic phosphate has no gamma radiation to complicate the health physics. Its 14.3 day half-life in contrast to that of 2.69 days for gold makes possible the use of much smaller total dosages. There were no untoward results from the use of this material. The results in the series here reported upon compare favorably with those reported for gold^{198}.

THERE ARE FEW CONDITIONS resulting from neoplastic processes that cause so much discomfort to the patient as the formation of pleural effusions and ascites. Often in the treatment of malignant disease, the relief of pain and discomfort is the best that can be achieved. Any new material or method that helps to do this is a valuable addition.

Radioactive chromic phosphate is a new material that is used to control effusions and ascites in the same fashion as is radioactive colloidal gold. The results with chromic phosphate are comparable to those with gold. The chromic phosphate has some advantages over gold, and a few disadvantages.

Radioactive gold for the control of ascites was first used by Muller, who reported his first work with it in 1949.[7] He had first used a radioactive isotope for this purpose in 1945. At that time he employed Zn_{63} (cyclotron prepared).[8]

In 1953, Seaman, Sherman and Bonebrake[11] reviewed the several reports that had appeared by then and found that favorable results varied from 30 per cent to 90 per cent in cases of malignant effusion in which radioactive gold was used. In their own series, 50 per cent of the patients treated had some measure of palliation. It is evident from these figures that the gold has value as an agent for palliation.

Since most (90 per cent) of the ionizing radiation from Au_{198} is due to the beta particles emitted, the gamma component only complicates the safety factors. The dosage scale for gold runs from 25 to 100 millicuries instilled into the pleural space, and 50 to 200 millicuries into the peritoneal cavity, at one administration. The equipment used for instillation is shown in Figure 1. The equipment and protection required, although not too complex or difficult, becomes much simpler when radioactive chromic phosphate is employed (Figure 2).

The dosage range for chromic phosphate runs between 6 and 9 millicuries for pleural effusions and between 9 and 12 millicuries for ascites.

The radioactivity of gold^{198} consists of an effective beta particle of 0.98 microvolts which has a maximum range of 3.8 mm. and a half path* of approximately 0.4 mm. in tissue, plus a gamma ray of 0.41 microvolts. After the injection, the patient becomes a source of radiation. It has been calculated that when 100 millicuries is placed in a peritoneal cavity, there is emitted from the patient 50 milliroentgens per hour at a distance of five feet. It is necessary, therefore, to keep such a patient at least six feet from other patients in order to stay within the maximum permissible daily radiation exposure; and a nurse, for example, may be within two feet of the patient for no more than 20 minutes each day.[2, 9]

The ionizing effect of radioactive chromic phosphate is due to the beta rays of P^{32} which have a maximum energy of 1.712 million electron volts. The energies of the beta rays average approximately 600,000 electron volts, but energies as high as 1,800,000 electron volts have been reported. In animal tissues, the beta ray has an average penetration of 2 mm. with a maximum of 7 mm. reported. The properties of and methods of preparation for the radioactive chromic phosphate are given herewith:

(a) Average particle size is 4 microns, with a range of 0.5 to 10 microns.

(b) The chromic phosphate is prepared to contain 1.0 millicuries P^{32} per ml. in sterile and pyrogen-free saline solution. The preparation contains approximately 3.5 mg. inert chromic phosphate (or 0.77 mg. P^{31}) per millicurie of radioactive phosphorus. Administration of 8 millicuries P^{32} is therefore also associated with the injection of 28 mg. of $CrPO_4$, or less than 0.5 mg. of $CrPO_4$ per kilogram of body weight. No toxic effects have ever been reported for the inactive chemical and the author would estimate the safety index to be in excess of 100. The method of preparation is as follows: To

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*Half the distance that a beta particle would penetrate in tissue before loss of all its energy.

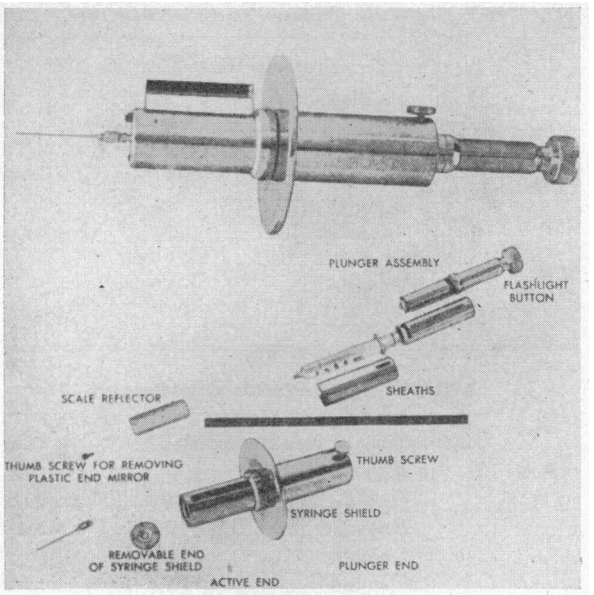

Figure 1.—Equipment used for instillation of gold[198].

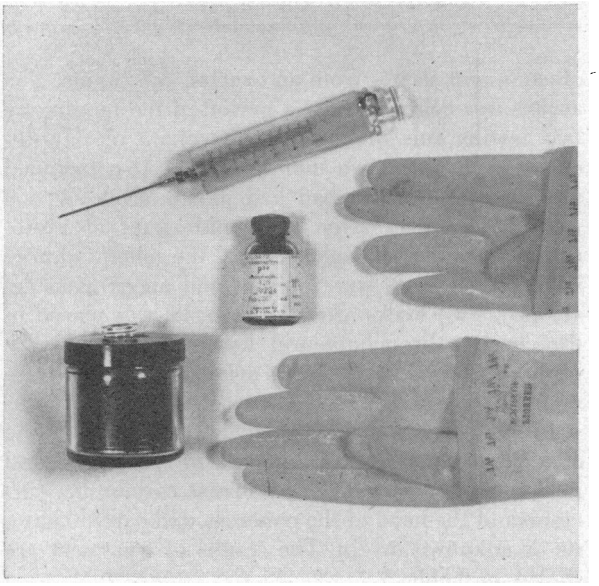

Figure 2.—Equipment needed for injection of radioactive chromic phosphate. The receptacle at lower left is a lead-lined glass bottle into which the bottle of chromic phosphate is placed.

the colloidal suspension of radioactive chromic phosphate is prepared by adding an equimolecular amount of chromic nitrate to radioactive phosphorus containing phosphoric acid carrier. The solution is evaporated to dryness and heated to 550° C. Pyrogen-free saline solution and pyrex glass beads are added and the preparation sterilized. The particles are reduced in size by shaking for 24 to 36 hours and the material is resterilized.[5, 6]

(c) Amorphous chromic phosphate is insoluble and appears to be biochemically inert. It therefore remains in situ, except for mechanical transport.

TABLE 1.—*Proportion of dose of P^{32} eliminated in urine and feces, as reported by Neukomm and co-workers*[10]

Number of days after injection	Percent of dose in urine and feces
5	0.36
12	0.11
19	0.05
26	0.04

The evidence to date indicates that such relocation takes place to a minor degree only, even with particles of less than one micron.[3]

The biological fate of the radioactive chromic phosphate has not been determined in all its phases.

Neukomm and co-workers[10] noted that when intratumoral injections of this material were used in the treatment of spontaneous mammary cancer in rats, part of the P^{32} was eliminated in the urine and feces in the proportions shown in Table 1.

It was assumed then that radioactive chromic phosphate, being insoluble and possessing only a beta component, could be used to treat serous effusions in the same manner as radioactive gold. Since the chromic phosphate had no gamma component, the need to protect personnel and patients from gamma radiation would be obviated and handling of the material and health physics would be simplified.

In the present series of cases, no quantitative determinations of uptake in the reticuloendothelial system were done. Nor were excretion studies carried out. However, no untoward effects or undesirable systemic effects were noted from the instillation of as much as 16 millicuries of radioactive chromic phosphate. The authors do not have proof that the material remains in situ, but the observations certainly suggest that it does, and that the ionizing effect is spent where the material comes into immediate contact with tumor cells in fluid and on exposed surfaces.

The technique employed for injection of radioactive chromic phosphate into the pleural space is as follows:

Thoracentesis is done and as much of the free fluid present as it is possible to remove is withdrawn. The suction apparatus is then detached from the needle and all equipment and drapes are removed from the field. The bottle containing the radioactive material is thoroughly shaken to obtain a uniform distribution of the particles. The bottle contains multiple small glass beads to facilitate this. The rubber stopper is cleaned with alcohol and the material is aspirated into a 10 cc. syringe. The syringe is detached from the aspirating needle and inserted into a thoracentesis needle and injection made into the free pleural space. Then the needle and syringe are withdrawn. The area is covered with 2 x 2 or 4 x 4 gauze pad and fastened with adhesive tape. The needle, barrel and plunger are separated and

wrapped in gauze and placed in a bag marked "contaminated." All contaminated linens are placed in bags and so marked, as are the rubber gloves worn by the physician throughout the procedure. The physician's hands are monitored for evidence of contamination. If activity is present on the hands, they are thoroughly and repeatedly washed in a detergent solution. All contaminated equipment and linen are removed to the "hot" laboratory where syringes and gloves are washed and then stored with the linens until the radioactive contamination has been spent and monitoring proves them "cold." This requires six to eight weeks, after which they may be returned to general use. Disposable materials are stored in a large can kept in an isolated area until sufficient time has elapsed for radioactive decay; then they may be burned.

The technique for instillation of the material into the abdominal cavity is essentially similar to that used for the chest, except that in some cases the material is diluted up to a volume of 50 or 100 cc. and instilled through polyethylene tubing with an outside dimension of 0.47 mm. The end of the tubing, which is perforated, is inserted into the peritoneal cavity through a No. 13 needle. Approximately 8 inches of the perforated end is passed into the abdomen. It is hoped by this means to obtain a better distribution of the radioactive material and to prevent pocketing.

From the foregoing it is evident that the chromic phosphate is simpler to use than Au^{198}. The danger to personnel and patients is lessened by the absence of a gamma component and by the smaller dosage requirements.

The means whereby the formation of fluid is suppressed is probably explained by the work of Goldie and co-workers.[4] They proved that intracavitary injections of radioactive gold have a lethal effect on free floating cells of sarcoma (S-37 and S-180). And the group at the Oak Ridge Institute for Nuclear Studies[1] noted that the presence of gold in serous cavities resulted in the disappearance of tumor cells from the fluid.

At the City of Hope, 25 cases of pleural effusion and 12 cases of ascites were treated.

The work was started in November 1952 and is continuing. Of the 25 cases of pleural effusion 17 were due to primary pulmonary neoplasms and eight were due to metastasis from primary lesions located outside the chest. Four of these were primary breast cancer, one testicular neoplasm, one kidney tumor, one rectal carcinoma and one ovarian carcinoma with both pleural effusion and ascites.

The results in the cases of pleural effusion are shown in Table 2.

The seven cases in which the treatment was ineffective included one in which there was both pleural effusion and ascites from an ovarian carcinoma. The ascites was controlled for a period of ten months by two instillations of chromic phosphate of 5 millicuries each given two months apart. Also included was one patient who had had pneumonectomy one week before instillation of 8 millicuries of radioactive chromic phosphate into the chest. Large mediastinal nodes were present and an effusion developed. Two weeks after the material was placed in the chest, a bronchopleural fistula developed. The health physics complications arising therefrom were numerous.

TABLE 2.—*Pleural effusions—Results of treatment*

Total number of patients treated	25	
Fluid controlled—		
1 month	4	
2 months	4	
3 months	5	
4 months	1	
6 months	2	
12 months	1	
15 months	1	
Failures	7	(28%)

TABLE 3.—*Ascites—Results of treatment*

Total number of patients treated	12	
Free of fluid—		
1 month	4	
2 months	2	
3 months	1	
4 months	1	
10 months	1	
Failures	3	(25%)

In the 12 cases of ascites treated, the cause of the condition was ovarian carcinoma in nine cases, and in one case of each primary breast carcinoma, carcinoma of the head of the pancreas and carcinomatosis of unknown origin. The results of treatment are shown in Table 3.

REPORTS OF TYPICAL CASES

Following are brief reports of typical cases:

CASE 1. A man 50 years of age had thoracotomy on November 24, 1953. One thousand cubic centimeters of clear yellow fluid was present and large hilar nodes were noted. A 6 cm. mass was present in the lingula of the left lung, which was adherent to the pericardium. A specimen was taken from the mass and the tissue removed was anaplastic epidermoid carcinoma. As the lesion was felt to be inoperable the chest was closed. On November 30, 1953, 9 millicuries of radioactive chromic phosphate was placed in the left side of the chest. About 300 cc. of fluid was present at the time. The patient remained comfortable and free of fluid until early in

February 1954. He was readmitted on February 12, 1954. Eight hundred cubic centimeters of clear fluid was aspirated from the left side of the chest and 8 millicuries of radioactive chromic phosphate was placed in the left pleural space. Fluid did not form thereafter.

CASE 2. A 58-year-old woman had a carcinoma of the breast removed in November 1951. In November 1952, left pleural effusion developed. Tumor cells were found in the effused fluid. On December 5, 1952, 8 millicuries of radioactive chromic phosphate was placed in the left chest cavity. The patient remained comfortable until July 1953, when fluid reaccumulated. She was then lost to follow-up and it was learned that she died on January 16, 1954.

CASE 3. A woman 57 years of age had laparotomy in March 1950 and bilateral ovarian carcinoma with peritoneal implants was observed. Postoperative radiation was administered. In February 1952 ascites developed, for which 5 millicuries of radioactive chromic phosphate was instilled into the peritoneal cavity. This was repeated in February 1953 for recurrence. The patient remained free of ascites until she died in December 1953. In November 1953, a pleural effusion developed, for which 8 millicuries of radioactive chromic phosphate was placed in the chest. Fluid recurred in the chest before the patient died.

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